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From efficacy to pragmatic trials: does the dodo bird verdict apply?



"Everybody has won, so all shall have prizes", concluded the dodo bird in *Alice in Wonderland* upon judging a race. Despite advances in treatment and the science upon which our treatments are built, the question of whether the dodo bird verdict continues to apply to our psychotherapy evidence¹ is emphasised by results of Ian Goodyer and colleagues' IMPACT trial in *The Lancet Psychiatry*.²

This pragmatic randomised controlled superiority trial compares three treatments in adolescents with unipolar major depressive disorder as delivered across diverse specialist mental health clinics in the UK health system: cognitive behavioural therapy (CBT), short-term psychoanalytical psychotherapy, and brief psychological intervention—the comparator treatment. Results indicate improvements over time for all three treatment conditions. However, the primary outcome of self-reported depressive symptoms, measured with the Mood and Feelings Questionnaire, did not differ significantly between groups at 36, 52, or 86 weeks post-randomisation, nor did the two hypothesised effective treatments (CBT and short-term psychoanalytical psychotherapy) lead to significantly greater benefits compared with the brief psychological intervention. Total costs of the trial interventions did not differ significantly between groups.

These results give the field a well needed jolt. Research advances have sparked efforts to move from bench to bedside and implement evidence-based treatments to improve patient outcomes. The long delays between scientific discoveries and translation into clinical practice have been tackled through various mechanisms, including systematic reviews, evidence-based treatment registries, and policies that encourage or incentivise evidence-based treatments.³ Yet results of this pragmatic trial point to similar effectiveness of three different treatment strategies varying in levels of supporting evidence.

CBT for depression has strong supporting evidence and is considered a well established treatment for adolescents with depression.³⁻⁵ Evidence is weaker for short-term psychoanalytical psychotherapy; to our knowledge, no randomised controlled trial has shown the efficacy of this intervention relative to a control or comparator

condition in adolescents with depression.^{2,6} In the IMPACT trial, the brief psychological intervention was delivered mostly by psychiatrists (84%), included known active treatment components from CBTs (eg, problem solving, encouragement of pleasant activities), and when combined with fluoxetine yielded effects similar to those noted for CBT, fluoxetine, and brief psychological intervention combined at 28 weeks in a previous study.⁷ The results of IMPACT raise questions about the effectiveness of all three treatments (combined with SSRIs in 36–41% of adolescents in each treatment group), and suggest that most psychotherapies will be "winners" on the basis of non-specific treatment factors, or alternatively that each treatment might contain distinct specific factors that contribute to recovery.

One caveat to consider in this trial is that passage of time might have accounted for improvements in clinical symptoms. The morbidity of adolescent depression ethically precludes a no-treatment comparator, but most major depressive episodes resolve over time, with recovery estimates as high as 90–100%.⁸⁻¹⁰ Although risk of relapse or recurrence (the study target) is high and estimated to be as high as 71%,^{9,10} the study endpoint (86 weeks post-randomisation, 52 weeks post-treatment) might have been too short to detect these effects.⁸

Pragmatic trials, such as IMPACT, evaluate treatments as delivered in routine practice, allowing for additions to the therapy under investigation—eg, treatment protocols, manuals, and treatment adherence monitoring. Treatment dose, training, and quality assurance protocols are often weaker in these trials than in highly controlled efficacy trials.³ Indeed, CBT adherence in IMPACT was modest relative to that for efficacy trials (74% of IMPACT CBT sessions met fidelity criteria vs 94–95% in the TORDIA study⁴), and the treatment adherence measure was not designed specifically for CBT. Although the tight control in efficacy trials done in highly controlled (often laboratory) settings, with rigorous therapist training and quality assurance monitoring, is crucial for identification of active treatment components and mechanisms, these controls are not generally achievable in routine specialist



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mental health clinics.³ What really matters to individuals living with depression is the benefits of treatments available in their clinics. Unfortunately, treatments as delivered in routine mental health settings and pragmatic trials might be less effective than in laboratory-based efficacy trials, with evidence pointing to stronger treatment effects when more efficacy design components are present.^{3,11}

Cross-national variability could also account for some differences between the IMPACT results and those of US trials in which CBT has frequently, but not always, shown advantages over strong comparator conditions, such as supportive therapy or family therapy.^{3-5,10} Variation exists across types of CBT for depression, and site differences are common in trials of depression treatment,¹² although are not apparent in the present study. The CBT given in IMPACT might have been less effective than that used in trials demonstrating efficacy. Review of the IMPACT adherence scales and CBT manual suggests that, compared with other types of CBT, the IMPACT model was more didactic, less youth friendly, and might have had less emphasis on elements viewed as preconditions for CBT efficacy (eg, therapist active listening and observation, collaborative agenda setting).^{4,8}

The IMPACT trial advances our knowledge and highlights directions for future research. If many of our treatments are “winners,” then a key task is to identify the elements that contribute to this common effectiveness. In our enthusiasm for translation of science to clinical practice, we might have overemphasised evidence-based treatments and not attended sufficiently to treatment processes that lead to efficacy of diverse treatments, such as the therapeutic alliance or monitoring of patient outcomes or using tools such as clinical dashboards to guide evidence-based decision making. Identification of treatments and treatment elements with minimal adverse effects is also important, and many adolescents continue to report depressive symptoms despite diagnostic remission in IMPACT and other trials.^{2,10} Consistent with personalised medicine, tailoring of treatments for individual young people might be crucial to achievement of optimal benefits. Genetic, hormonal, brain-imaging, stress, and other forthcoming data

from the IMPACT trial will enable analyses exploring variation and mechanisms of treatment response, enhancing knowledge for personalised approaches and the innovative contributions of this study. Finally, more research aimed at understanding key elements and mechanisms contributing to treatment effectiveness are needed in both controlled and pragmatic trials before a firm conclusion regarding the dodo bird verdict is applied.

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We declare no competing interests.

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